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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,788	KATO ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,11,13-17 and 19* is/are pending in the application.

4a) Of the above claim(s) *11,13-17 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 9/8/2009 is acknowledged and has been entered. Claims 1-5, 7, 11, 13-17 and 19 are pending. Claims 11, 13-17 and 19 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-5 and 7 are discussed in this Office action. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

The Examiner acknowledges Applicant's arguments concerning the claim to priority. It is noted that foreign priority was acknowledged on the BIB data sheet in PAIR and is further acknowledged in this Office action (see form PTOL-326).

Previous Rejections

3. The prior art rejections under 35 USC 102(b) are maintained and discussed below. The prior art rejections under 35 USC 103(a) are maintained and discussed below.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-5 and 7 are finally rejected under 35 U.S.C. 102(b) as being anticipated by Kato et al (W0 94/08001, April 1994, US equivalent 5597713, January 1997). Regarding claim 1, Kato et al teach a method constructing a DNA vector having a cDNA synthesized from a mRNA, the method comprising annealing a double stranded DNA primer and an mRNA mixture, wherein the double stranded DNA primer contains a replication origin; preparing an mRNA/cDNA heteroduplex by synthesizing a first-strand cDNA primed with the double stranded DNA primer using reverse transcriptase; circularizing the mRNA/cDNA using T4 RNA ligase to form a circular mRNA/cDNA heteroduplex and replacing the RNA in the mRNA/cDNA heteroduplex with a second strand cDNA by synthesizing the second -strand cDNA with a DNA polymerase, thereby constructing the DNA vector having the cDNA consisting of the first-strand cDNA and the second-strand cDNA (see entire patents, especially col. 3-6).

Regarding claim 2, Kato et al teach wherein the RNA is in a cell extract (col. 3, lines 16-17 and Examples beginning at col. 6 and especially Figure 2).

Regarding claim 3, Kato et al teach the method of claim 1, wherein mRNA possessing a cap structure is synthesized by in vitro transcription (col. 2-3).

Regarding claim 4, Kato et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains a sequence complementary to a partial sequence of mRNA possessing a cap structure (Figure 2 and col. 2-4).

Regarding claim 5, Kato et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains an oligo dT complementary to a poly(A) sequence of mRNA possessing a cap structure (figure 2, and col. 2-4).

Regarding claim 7, Kato al teach the method of claim 1, which comprises the following step between the step (ii) and the step (iii): (ii') generating a 5'-protruding end or a blunt end at the terminal of the double-stranded DNA primer by cutting the conjugate of the mRNA/cDNA heteroduplex and the double-stranded DNA primer using a restriction enzyme (col. 3-6). Therefore, Kato et al meet the limitations of the claims as currently written.

Response to Arguments

6. Applicant traverses the rejections on the following ground: Applicant states that Kato comprises a first end of "DNA/DNA" and a second end of "DNA/DNA". Applicant state see figure 1 of 2 of Kato et al. Applicant states that Kato ligated the DNA/DNA and the second DNA/DNA to forma a circular vector containing the mRNA/cDNA heteroduplex. Applicant states that Kato uses t4 DNA ligase rather than tT4 RNA ligase. Applicant states that Kato ligates DNA and DNA using the T4 DNA ligase. The t$ ligase of Kato et al is used for ligating the DNA-RNA chimeric oligonucleotide with mRNA, but circularizing the heteroduplex is performed with T4 DNA ligase. Applicant states that even though Kato does not explicitly describe the use of T4 DNA ligase for circularization, such is common knowledge in the art for ligating DNA and

DNA. Applicant finally states that Kato fails to teach that the first linear end of the heteroduplex is mRNA/cDNA and the second linear end is DNA/DNA.

All of the arguments have been thoroughly review and considered but are not found persuasive for the reasons that follow: In regards to Applicant's arguments concerning the teaching of Kato et al, the Examiner does not see wherein a DNA/DNA is ligated to DNA/DNA. Nowhere in the Figures 1 and 2 (noted by Applicant) are there any teachings of DNA/DNA ligated to DNA/DNA. Kato et al expressly teach at col. 3, lines 4-13, that the first process consists of ligation of a DNA oligonucleotide or a DNA RNA chimeric oligonucleotide to an intact mRNA possessing a cap and the second process consist of cDNA synthesis from the synthetic oligonucleotide-capped mRNA and production of a recombinant vector contain the cDNA. Likewise it is noted that the Examiner did not find wherein T4 DNA ligase was used to form the circular vector as argued by Applicant. Thus, this argument is not found persuasive. Additionally concerning the common knowledge argument, Applicant provides no evidence to support this conclusion.

Further contrary to Applicant's arguments, the prior art recognize that T4 RNA ligase can couple single stranded DNA or RNA (see Kool; col. 11, lines 33-34). In fact, Kool (US 6368802, April 2002) teaches that circularization of oligonucleotides can be carried out enzymatically, using T4 DNA ligase and a short adaptor oligomer which is complementary to the ends being joined or using T4 RNA ligase without an adaptor (see col. 33, lines 44-45 to col. 34, lines 1-2). Thus, Applicant's arguments are not found persuasive to overcome the prior art rejection noted above.

Claim Rejections - 35 USC § 103

7. . The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-5 and 7 are finally rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik et al (5962271, citation made of record in prior Office action) in view of Brennan et al (Methods in Enzymology, vol. 100, pages 38-52, 1983). Regarding claim 1, Chenchik et al teach a method comprising the steps of: (i) annealing a double-stranded DNA primer and an mRNA mixture, (ii) preparing an mRNA/cDNA heteroduplex by synthesizing the first-strand cDNA primed with the double-stranded DNA primer using reverse transcriptase, wherein the 3' end nucleotide of the first strand cDNA comprise an anchor (see for example Figure 1), (iii) circularizing the mRNA/cDNA heteroduplex by joining the 3' and 5' ends of the DNA strand containing cDNA using ligase and replacing the RNA in the mRNA/cDNA heteroduplex with the second strand cDNA thereby synthesizing the cDNA (see figure 4-1 and 4-2, col. 3-5, 7-9 and Examples; see also col. 8, line 61 to col. 9, line 13) possessing the 5' end nucleotide cap structure comprising the formula dN_1-dN_2-....dNm-rN_1-rN2....rNn, wherein dN represents a deoxyribonucleotide selected from among dAMP, dCMP, dGMP and dTMP; m represents an integer 0 and above, preferably from 10-50; rN represents a

ribonucleotide selected from among AMP, CMP, GMP and UMP, preferably GMP; and n represents an integer 0 and above, preferably from 3 to 7 (col. 3, line 50 to col. 4, line 50).

Chenchick et al do not teach wherein the ligase is T4 RNA ligase, but rather wherein the ligase is T4 DNA ligase.

Brennan et al provide a general teaching T4 RNA ligases. Brennan et al teach that although RNA ligases uses oligoribonucleotides much more efficiently than oligodeoxyribonucleotides, short DNA oligomers can be both circularized and joined imtermolecularly (page 39, second paragraph).

Kato supports the teachings of Brennan by disclosing wherein T4 RNA ligase is used for ligation of DNA-RNA chimeric oligonucleotide to mRNA (col. 3, lines 47-64).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to substitute T4 RNA ligase as taught by Brennan and Kato in the place of the T4 DNA ligase in the synthesis method of Chenchik since the ordinary artisan has good reasons to peruse the known options within his or her technical grasp and further since the use of T4 RNA ligase does not negatively alter, modify or disrupt the method of synthesis method of Chenchik. In turn, because T4 RNA ligase is known to ligate DNA oligonucleotides, RNA oligonucleotides or chimeric oligonucleotides comprising RNA-DNA to mRNA as taught by Brennan and Kato, one of ordinary skill in the art at the time of the claimed invention could predictably expect a reasonable expectation of success in the DNA synthesis method of Chenchik.

Regarding claim 2, Chenchik et al teach that the small amount of total RNA from 10-50 mg of "difficult" cells or tissues, like human biopsy tissues, pathogenic microorganisms, and tissues at different development stages and so on (col. 11, lines 32-35). One of ordinary skill in the art at the time of the claimed invention would have a reasonable expectation of success in obtaining mRNA contained in a cell extract for use in methods of synthesizing cDNA possessing a cap structured based on the teachings of Chenchik et al. It would have been *prima facie* obvious over the cited prior arts in the absence of secondary consideration.

Regarding claim 3, Chenchik et al teach the method of claim 1, wherein mRNA possessing a cap structure is synthesized by in vitro transcription (col. 5, lines 11-53, and claim 1).

Regarding claim 4, Chenchik et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains a sequence complementary to a partial sequence of mRNA possessing a cap structure (see col. 7, line 52 to col. 8, line 43).

Regarding claim 5, Chenchik et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains an oligo dT complementary to a poly(A) sequence of mRNA possessing a cap structure (col. 7, lines 50-56).

Regarding claim 7, Chenchik et al teach the method of claim 1, which comprises the following step between the step (ii) and the step (iii): (ii') generating a 5'-protruding

end or a blunt end at the terminal of the double-stranded DNA primer by cutting the conjugate of the mRNA/cDNA heteroduplex and the double-stranded DNA primer using a restriction enzyme (col. 11, Example 2).

Response to Arguments

9. Applicant traverses the rejection on the following grounds: Applicant traverses the rejection on the grounds that one could not substitute the T4 RNA ligase of Brennan into the method of Chenchick because T4 cannot be used to form such circular vector in such a heteroduples. Applicant states that such combination would be expected to be ineffective to form circular vector.

All of the arguments have been thoroughly reviewed and considered, but it is noted that Applicant provides no evidence to support the conclusions noted above. MPEP states that the arguments of counsel cannot take the place of evidence in the record. *In re Schulze,* 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant (see MPEP 716.01 (b). For these reasons and the reasons already made of record, the rejections are maintained.

Conclusion

10. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637